

# Rogaine<sup>®</sup>

TOPICAL  
SOLUTION

minoxidil 2%



## For Women

The First  
Medication  
Proven  
Effective  
For The  
Treatment  
Of Hair Loss  
In Women



**Rogaine<sup>®</sup>**  
Real Help For Some Women With Hair Loss

**Upjohn**

DERMATOLOGY  
DIVISION

Please see adjacent page  
for brief summary of prescribing information.

©1992 The Upjohn Company

For the many faces of mild hypertension

# MILD

THE MOST WIDELY USED CALCIUM ANTAGONIST  
AS MONOTHERAPY FOR MILD HYPERTENSION\*

- Effective 24-hour control<sup>2</sup>
- Single-agent efficacy
- Well tolerated<sup>†</sup>
- No adverse effects on total cholesterol, plasma glucose, or renal function<sup>‡</sup>

ONCE-DAILY  
**Calan<sup>®</sup> SR**  
Verapamil HCl

\*The recommended starting dose for Calan SR is 180 mg once daily. Dose titration will be required in some patients to achieve blood pressure control. A lower initial starting dosage of 120 mg/day may be warranted in some patients (eg, the elderly, patients of small stature). Dosages above 240 mg daily should be administered in divided doses. Calan SR should be administered with food.

†Constipation, which is easily managed in most patients, is the most commonly reported side effect of Calan SR.

‡Verapamil should be administered cautiously to patients with impaired renal function.

#### BRIEF SUMMARY

**Contraindications:** Severe LV dysfunction (see *Warnings*), hypotension (systolic pressure < 90 mm Hg) or cardiogenic shock, sick sinus syndrome (if no pacemaker is present), 2nd- or 3rd-degree AV block (if no pacemaker is present), atrial flutter/fibrillation with an accessory bypass tract (eg, WPW or LGL syndromes), hypersensitivity to verapamil.

**Warnings:** Verapamil should be avoided in patients with severe LV dysfunction (eg, ejection fraction < 30%) or moderate to severe symptoms of cardiac failure and in patients with any degree of ventricular dysfunction if they are receiving a beta-blocker. Control milder heart failure with optimum digitalization and/or diuretics before Calan SR is used. Verapamil may occasionally produce hypotension. Elevations of liver enzymes have been reported. Several cases have been demonstrated to be produced by verapamil. Periodic monitoring of liver function in patients on verapamil is prudent. Some patients with paroxysmal and/or chronic atrial flutter/fibrillation and an accessory AV pathway (eg, WPW or LGL syndromes) have developed an increased antegrade conduction across the accessory pathway bypassing the AV node, producing a very rapid ventricular response or ventricular fibrillation after receiving I.V. verapamil (or digitalis). Because of this risk, oral verapamil is contraindicated in such patients. AV block may occur (2nd- or 3rd-degree, 0.8%). Development of marked 1st-degree block or progression to 2nd- or 3rd-degree block requires reduction in dosage or, rarely, discontinuation and institution of appropriate therapy. Sinus bradycardia, 2nd-degree AV block, sinus arrest, pulmonary edema and/or severe hypotension were seen in some critically ill patients with hypertrophic cardiomyopathy who were treated with verapamil.

**Precautions:** Verapamil should be given cautiously to patients with impaired hepatic function (in severe dysfunction use about 30% of the normal dose) or impaired renal function, and patients should be monitored for abnormal prolongation of the PR interval or other signs of overdosage. Verapamil may decrease neuromuscular transmission in patients with Duchenne's muscular dystrophy and may prolong recovery from the neuromuscular blocking agent vecuronium. It may be necessary to decrease verapamil dosage in patients with attenuated neuromuscular transmission. Combined therapy with beta-adrenergic blockers and verapamil may result in additive negative effects on heart rate, atrioventricular conduction and/or cardiac contractility; there have been reports of excessive bradycardia and AV block, including complete heart block. The risks of such combined therapy may outweigh the benefits. The combination should be used only with caution and close monitoring. Decreased metoprolol and propranolol clearance may occur when either drug is administered concomitantly with verapamil. A variable effect has been seen with combined use of atenolol. Chronic verapamil treatment can increase serum digoxin levels by 50% to 75% during the first week of therapy, which can result in digitalis toxicity. In patients with hepatic cirrhosis, verapamil may reduce total body clearance and extrarenal clearance of digoxin. The digoxin dose should be reduced when verapamil is given, and the patient carefully

**References:** 1. Data on file, Searle. 2. Edmonds D, Würth JP, Baumgart P, et al. Twenty-four-hour monitoring of blood pressure during calcium antagonist therapy. In: Fleckenstein A, Laragh SH, eds. *Hypertension—the Next Decade: Verapamil in Focus*. New York, NY: Churchill Livingstone; 1987:94-100. 3. Midtbo KA. Effects of long-term verapamil therapy on serum lipids and other metabolic parameters. *Am J Cardiol*. 1990;66:131-151. 4. Fagher B, Henningsen N, Hulthén L, et al. Antihypertensive and renal effects of enalapril and slow-release verapamil in essential hypertension. *Eur J Clin Pharmacol*. 1990;39(suppl 1):S41-S43. 5. Schmieder RE, Messerli FH, Caravaglia GE, et al. Cardiovascular effects of verapamil in patients with essential hypertension. *Circulation*. 1987;75:1030-1036. 6. Midtbo K, Lauve O, Hals O. No metabolic side effects of long-term treatment with verapamil in hypertension. *Angiology*. 1988;39:1025-1029.

monitored. Verapamil will usually have an additive effect in patients receiving blood-pressure-lowering agents. Disopyramide should not be given within 48 hours before or 24 hours after verapamil administration. Concomitant use of flecainide and verapamil may have additive effects on myocardial contractility, AV conduction, and repolarization. Combined verapamil and quinidine therapy in patients with hypertrophic cardiomyopathy should be avoided, since significant hypotension may result. Concomitant use of lithium and verapamil may result in a lowering of serum lithium levels or increased sensitivity to lithium. Patients receiving both drugs must be monitored carefully. Verapamil may increase carbamazepine concentrations during combined use. Rifampin may reduce verapamil bioavailability. Phenobarbital may increase verapamil clearance. Verapamil may increase serum levels of cyclosporin. Verapamil may inhibit the clearance and increase the plasma levels of theophylline. Concomitant use of inhalation anesthetics and calcium antagonists needs careful titration to avoid excessive cardiovascular depression. Verapamil may potentiate the activity of neuromuscular blocking agents (curare-like and depolarizing); dosage reduction may be required. There was no evidence of a carcinogenic potential of verapamil administered to rats for 2 years. A study in rats did not suggest a tumorigenic potential, and verapamil was not mutagenic in the Ames test. Pregnancy Category C. There are no adequate and well-controlled studies in pregnant women. This drug should be used during pregnancy, labor, and delivery only if clearly needed. Verapamil is excreted in breast milk; therefore, nursing should be discontinued during verapamil use.

**Adverse Reactions:** Constipation (7.3%), dizziness (3.3%), nausea (2.7%), hypotension (2.5%), headache (2.2%), edema (1.9%), CHF, pulmonary edema (1.8%), fatigue (1.7%), dyspnea (1.4%), bradycardia: HR < 50/min (1.4%), AV block: total 1°, 2°, 3° (1.2%), 2° and 3° (0.8%), rash (1.2%), flushing (0.6%), elevated liver enzymes, reversible non-obstructive paralytic ileus. The following reactions, reported in 1.0% or less of patients, occurred under conditions where a causal relationship is uncertain: angina pectoris, atrioventricular dissociation, chest pain, claudication, myocardial infarction, palpitations, purpura (vasculitis), syncope, diarrhea, dry mouth, gastrointestinal distress, gingival hyperplasia, ecchymosis or bruising, cerebrovascular accident, confusion, equilibrium disorders, insomnia, muscle cramps, paresthesia, psychotic symptoms, shakiness, somnolence, arthralgia and rash, exanthema, hair loss, hyperkeratosis, macules, sweating, urticaria, Stevens-Johnson syndrome, erythema multiforme, blurred vision, gynecostasia, galactorrhea/hyperprolactinemia, increased urination, spotty menstruation, impotence.

4/11/91 • P91CA6277V

Address medical inquiries to:  
G.D. Searle & Co.  
Medical & Scientific  
Information Department  
4901 Searle Parkway  
Skokie, IL 60077


**SEARLE**


G.D. Searle & Co.  
Box 5170, Chicago, IL 60680

# 1-800-ASK-PACE

## LAPAROSCOPY IS ONE WAY OUR PHYSICIANS VIEW SURGERY.





 With **1-800-ASK-PACE**, Physician Access and Communication Exchange, the Department of Surgery at the distinguished new USC University Hospital can now be a vitally important extension of your practice.

 Our surgical faculty, all from the USC School of Medicine, have expertise in a wide variety of minimally invasive (laparoscopic) surgical procedures such as cholecystectomy, hernia surgery, appendectomy, antireflux surgery, esophageal myotomy and bowel resection.

 If you have a patient who could benefit from

minimally invasive surgery, **PACE** can help. As a physician-to-physician service, **1-800-ASK-PACE** links you to the right physician for consultations and patient transfers.

 Our **PACE** representatives are specially trained to quickly connect you with the physician or resource you require and will stay with you until you are satisfied with the result.

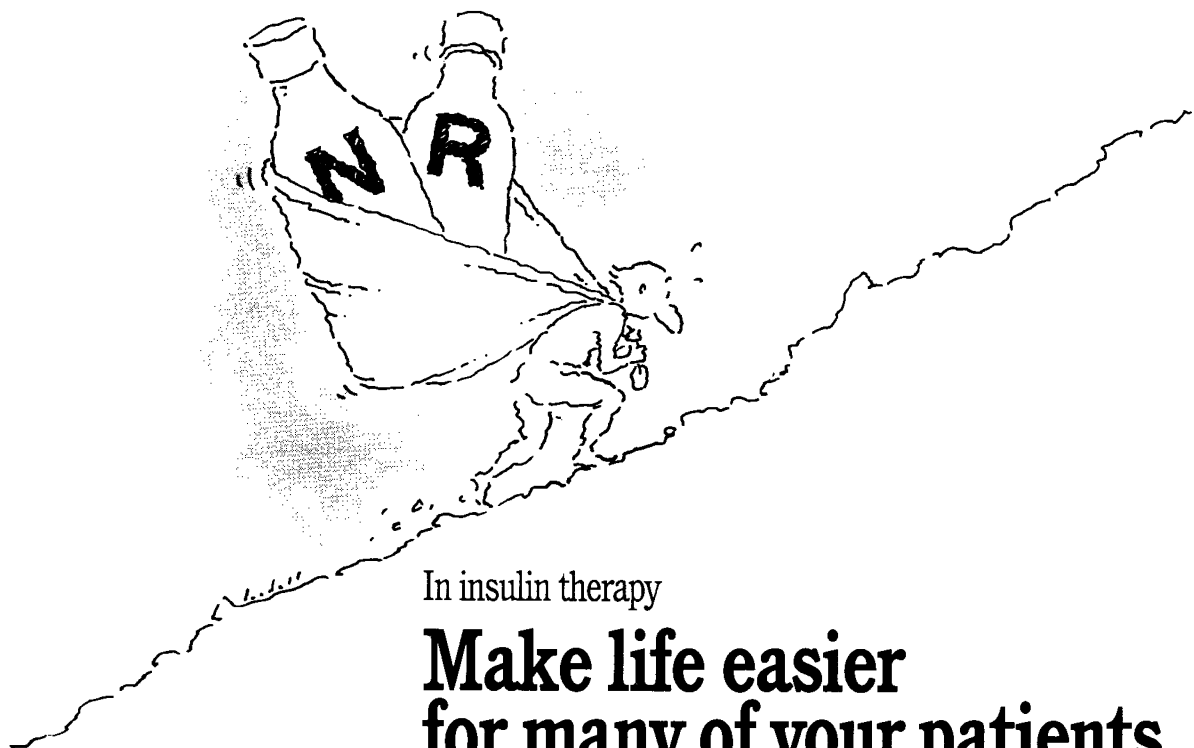
 Whether it's a consult, patient status, clinical or laboratory services or the latest research data, simply pick up the phone and dial, **1-800-ASK-PACE** (275-7223). We'll put our medical/surgical expertise on the line.



**USC UNIVERSITY HOSPITAL**  
Richard K. Eamer Medical Plaza

We're advancing medicine.

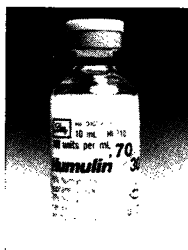
A National Medical Enterprises Medical Center.



In insulin therapy

## Make life easier for many of your patients

Humulin 70/30. Convenient and simple to administer.



No more mixing. No more mixing errors.  
All of which makes living with diabetes a  
little easier for patients. And compliance  
a lot easier to achieve.

# Humulin<sup>®</sup> 70/30

70% human insulin isophane suspension  
30% human insulin injection  
(recombinant DNA origin)



*Global Excellence in Diabetes Care*

**Eli Lilly and Company**  
Indianapolis, Indiana  
46285

*The patient-friendly premix*

**WARNING:** Any change of insulin should be made cautiously and only  
under medical supervision.

# ONCE-A-DAY CARDIZEM® CD

(diltiazem HCl)

NOW AVAILABLE ON  
MEDI-CAL  
for Your Prescribing  
Convenience  
180mg 3080M 240mg 3080N 300mg 3080P

## ONE TO SWITCH TO

Easy to switch from Cardizem® SR  
(diltiazem HCl) on a total mg/day basis

Convenient once-a-day dosage  
for proven 24-hour control<sup>1</sup>

A favorable side-effect profile<sup>1</sup>

Once-a-day dosing schedules result  
in improved compliance<sup>2</sup>

### LOWER PRICE\*

25% lower cost than  
Cardizem® SR capsules

- Cardizem SR is available in 60-, 90- and 120-mg capsules

### Flexible dosage range

- Start with one 180-mg capsule daily
- Available in 180-, 240-, and 300-mg capsules

\* Based on AWP prices.

Cardizem CD is indicated for  
the treatment of hypertension.

Please see brief summary of  
prescribing information on  
next page.



 MARION MERRELL DOW INC.  
PRESCRIPTION PRODUCTS DIVISION  
KANSAS CITY, MO 64114

# ONCE-A-DAY CARDIZEM® CD

(diltiazem HCl)

CCDAH584/A6918

6521H2



# ONCE-A-DAY CARDIZEM<sup>®</sup> CD (diltiazem HCl)

**Switch from Cardizem<sup>®</sup> SR on a total mg/day basis  
For new patients starting on Cardizem<sup>®</sup> CD:**

- Start with one 180-mg capsule daily
- Monitor for 2 weeks
- If necessary, titrate to goal blood pressure

## BRIEF SUMMARY

CARDIZEM<sup>®</sup> CD (diltiazem hydrochloride) Capsules  
CARDIZEM<sup>®</sup> SR (diltiazem hydrochloride) Sustained Release Capsules

## CONTRAINDICATIONS

CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, (3) patients with hypotension (less than 90 mm Hg systolic), (4) patients who have demonstrated hypersensitivity to the drug, and (5) patients with acute myocardial infarction and pulmonary congestion documented by X-ray on admission.

## WARNINGS

**1. Cardiac Conduction.** CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (13 of 3,007 patients or 0.43%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of diltiazem.

**2. Congestive Heart Failure.** Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt). An acute study of oral diltiazem in patients with impaired ventricular function (ejection fraction 24% ± 6%) showed improvement in indices of ventricular function without significant decrease in contractile function (dp/dt). Worsening of congestive heart failure has been reported in patients with preexisting impairment of ventricular function. Experience with the use of CARDIZEM in combination with beta-blockers in patients with impaired ventricular function is limited. Caution should be exercised when using this combination.

**3. Hypotension.** Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.

**4. Acute Hepatic Injury.** Mild elevations of transaminases with and without concomitant elevation in alkaline phosphatase and bilirubin have been observed in clinical studies. Such elevations were usually transient and frequently resolved even with continued diltiazem treatment. In rare instances, significant elevations in enzymes such as alkaline phosphatase, LDH, SGOT, SGPT, and other phenomena consistent with acute hepatic injury have been noted. These reactions tended to occur early after therapy initiation (1 to 8 weeks) and have been reversible upon discontinuation of drug therapy. The relationship to CARDIZEM is uncertain in some cases, but probable in some. (See PRECAUTIONS.)

## PRECAUTIONS

**General.** CARDIZEM is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these changes were reversible with continued dosing.

Dermatologic events (see ADVERSE REACTIONS section) may be transient and may disappear despite continued use of CARDIZEM. However, skin eruptions progressing to erythema multiforme and/or exfoliative dermatitis have also been infrequently reported. Should a dermatologic reaction persist, the drug should be discontinued.

**Drug Interaction.** Due to the potential for additive effects, caution and careful titration are warranted in patients receiving CARDIZEM concomitantly with any agents known to affect cardiac contractility and/or conduction. (See WARNINGS.) Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS.)

As with all drugs, care should be exercised when treating patients with multiple medications. CARDIZEM undergoes biotransformation by cytochrome P-450 mixed function oxidase. Coadministration of CARDIZEM with other agents which follow the same route of biotransformation may result in the competitive inhibition of metabolism. Doses of similarly metabolized drugs such as cyclosporin, particularly those of low therapeutic ratio or in patients with renal and/or hepatic impairment, may

require adjustment when starting or stopping concomitantly administered CARDIZEM to maintain optimum therapeutic blood levels.

**Beta-blockers:** Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers is usually well tolerated, but available data are not sufficient to predict the effects of concomitant treatment in patients with left ventricular dysfunction or cardiac conduction abnormalities.

Administration of CARDIZEM concomitantly with propranolol in five normal volunteers resulted in increased propranolol levels in all subjects and bioavailability of propranolol was increased approximately 50%. If combination therapy is initiated or withdrawn in conjunction with propranolol, an adjustment in the propranolol dose may be warranted. (See WARNINGS.)

**Cimetidine:** A study in six healthy volunteers has shown a significant increase in peak diltiazem plasma levels (58%) and area-under-the-curve (53%) after a 1-week course of cimetidine at 1,200 mg per day and diltiazem 60 mg per day. Ranitidine produced smaller, nonsignificant increases. The effect may be mediated by cimetidine's known inhibition of hepatic cytochrome P-450, the enzyme system probably responsible for the first-pass metabolism of diltiazem. Patients currently receiving diltiazem therapy should be carefully monitored for a change in pharmacological effect when initiating and discontinuing therapy with cimetidine. An adjustment in the diltiazem dose may be warranted.

**Digitalis:** Administration of CARDIZEM with digoxin in 24 healthy male subjects increased plasma digoxin concentrations approximately 20%. Another investigator found no increase in digoxin levels in 12 patients with coronary artery disease. Since there have been conflicting results regarding the effect of digoxin levels, it is recommended that digoxin levels be monitored when initiating, adjusting, and discontinuing CARDIZEM therapy to avoid possible over- or under-digitalization. (See WARNINGS.)

**Anesthetics:** The depression of cardiac contractility, conductivity, and automaticity as well as the vascular dilation associated with anesthetics may be potentiated by calcium channel blockers. When used concomitantly, anesthetics and calcium blockers should be titrated carefully.

**Carcinogenesis, Mutagenesis, Impairment of Fertility.** A 24-month study in rats at oral dosage levels of up to 100 mg/kg/day, and a 21-month study in mice at oral dosage levels of up to 30 mg/kg/day showed no evidence of carcinogenicity. There was also no mutagenic response in vitro or in vivo in mammalian cell assays or in vitro in bacteria. No evidence of impaired fertility was observed in a study performed in male and female rats at oral dosages of up to 100 mg/kg/day.

**Pregnancy.** Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/postnatal studies, there was an increased incidence of stillbirths at doses of 20 times the human dose or greater.

There are no well-controlled studies in pregnant women; therefore, use of CARDIZEM in pregnant women only if the potential benefit justifies the potential risk to the fetus.

**Nursing Mothers.** Diltiazem is excreted in human milk. One report suggests that concentrations in breast milk may approximate serum levels. If use of CARDIZEM is deemed essential, an alternative method of infant feeding should be instituted.

**Pediatric Use.** Safety and effectiveness in children have not been established.

## ADVERSE REACTIONS

Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded from these studies.

The adverse events described below represent events observed in clinical studies of hypertensive patients receiving either CARDIZEM Tablets or CARDIZEM SR Capsules as well as experiences observed in studies of angina and during marketing. The most common events in hypertension studies are shown in a table with rates in placebo patients shown for comparison. Less common events are listed by body system; these include any adverse reactions seen in angina studies that were not observed in hypertension studies. In all hypertensive patients taking CARDIZEM Tablets or CARDIZEM SR Capsules (total over 900), the most common adverse events were edema (9%), headache (8%), dizziness (6%), asthenia (5%), sinus bradycardia (3%), flushing (3%), and first-degree AV block (3%). Only edema and perhaps bradycardia and dizziness were dose related.

## DOUBLE BLIND PLACEBO CONTROLLED HYPERTENSION TRIALS

ADVERSE	DILTIAZEM N=315 # PTS (%)	PLACEBO N=211 # PTS (%)
Headache	38 (12%)	17 (8%)
AV Block First Degree	24 (7.6%)	4 (1.9%)
Dizziness	22 (7%)	6 (2.8%)
Edema	19 (6%)	2 (0.9%)
Bradycardia	19 (6%)	3 (1.4%)
ECG Abnormality	13 (4.1%)	3 (1.4%)
Asthenia	10 (3.2%)	1 (0.5%)
Constipation	5 (1.6%)	2 (0.9%)
Dyspepsia	4 (1.3%)	1 (0.5%)
Nausea	4 (1.3%)	2 (0.9%)
Palpitations	4 (1.3%)	2 (0.9%)
Polyuria	4 (1.3%)	2 (0.9%)
Somnolence	4 (1.3%)	—
Alk Phos Increase	3 (1%)	1 (0.5%)
Hypotension	3 (1%)	1 (0.5%)
Insomnia	3 (1%)	1 (0.5%)
Rash	3 (1%)	1 (0.5%)
AV Block Second Degree	2 (0.6%)	—

The following table presents the most common adverse reactions reported in placebo-controlled trials in patients receiving CARDIZEM CD up to 360 mg with rates in placebo patients shown for comparison.

ADVERSE REACTION	CARDIZEM CD N=324	PLACEBO N=175
HEADACHE	9.0%	8.0%
BRADYCARDIA	4.3%	2.3%
EDEMA	3.7%	2.3%
DIZZINESS	3.1%	3.4%
ECG ABNORMALITY	3.1%	2.9%
AV BLOCK FIRST DEGREE	2.2%	—
ASTHENIA	1.9%	1.7%

In clinical trials of CARDIZEM CD Capsules, CARDIZEM Tablets, and CARDIZEM SR Capsules involving over 3000 patients, the most common events (ie, greater than 1%) were edema (4.9%), headache (4.9%), dizziness (3.5%), asthenia (2.7%), first-degree AV block (2.2%), bradycardia (1.6%), flushing (1.5%), nausea (1.4%), rash (1.3%), and dyspepsia (1.2%).

In addition, the following events were reported infrequently (less than 1%).

**Cardiovascular:** Angina, arrhythmia, AV block (second- or third-degree), bundle branch block, congestive heart failure, ECG abnormalities, hypotension, palpitations, syncope, tachycardia, ventricular extrasystoles.

**Nervous System:** Abnormal dreams, amnesia, depression, gait abnormality, hallucinations, insomnia, nervousness, paresthesia, personality change, somnolence, thirst, vomiting, weight increase.

**Gastrointestinal:** Anorexia, constipation, diarrhea, dry mouth, dysgeusia, mild elevations of SGOT, SGPT, LDH, and alkaline phosphatase (see hepatic warnings), thirst, vomiting, weight increase.

**Dermatological:** Patches, photosensitivity, pruritus, urticaria.

**Other:** Amblyopia, CPK increase, dyspnea, epistaxis, eye irritation, hyperglycemia, hyperuricemia, impotence, muscle cramps, nasal congestion, nocturia, osteoarthritis, polyuria, sexual difficulties.

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: alopecia, erythema multiforme, exfoliative dermatitis, extrapyramidal symptoms, gingival hyperplasia, hemolytic anemia, increased bleeding time, leukopenia, purpura, retinopathy, and thrombocytopenia. In addition, events such as myocardial infarction have been observed which are not readily distinguishable from the natural history of the disease in these patients. A number of well-documented cases of generalized rash, characterized as leukocytoclastic vasculitis, have been reported. However, a definitive cause and effect relationship between these events and CARDIZEM therapy is yet to be established.

## HOW SUPPLIED

CARDIZEM<sup>®</sup> CD (diltiazem hydrochloride) is available as capsules of 180 mg, 240 mg, and 300 mg in bottles of 30 and 90, and in UDIP<sup>®</sup> packages of 100.

CARDIZEM<sup>®</sup> SR (diltiazem hydrochloride) is available as sustained release capsules of 60 mg, 90 mg, and 120 mg in bottles of 100, and in UDIP<sup>®</sup> packages of 100.

CARDIZEM<sup>®</sup> CD Product Information as of October 1991

CARDIZEM<sup>®</sup> SR Product Information as of January 1991

**References:** 1. Data on file, Marion Merrell Dow Inc. 2. Cramer JA, Mattson RH, Prevey ML, et al. JAMA. 1989;261(22):3273-3274.



MARION MERRELL DOW INC.  
PRESCRIPTION PRODUCTS DIVISION  
KANSAS CITY, MO 64114

## Announcing Journal Watch - The Audio Cassette Service - the fastest way to keep up with what's new and important in medicine

Twice a month, **Journal Watch — The Audio Cassette Service** brings you 60 minutes of clear, concise summaries of the latest advances published in more than 20 major journals.

**Journal Watch — The Audio Cassette Service** is written exclusively by practicing physicians. With your subscription you can earn two Category I CME credits per one hour program — at no additional cost.

Using **Journal Watch's** convenient, easy to listen to audio cassettes, you can schedule when and where to listen.

In your car  
At the gym  
During meal time  
Between patients  
During your daily routines  
Or simply spare moments of the day

Brought to you by two leaders in medical information — **Audio-Digest Foundation**, producers of "The Thirteen Spoken Medical Journals®" and the **Massachusetts Medical Society**, publishers of the *New England Journal of Medicine*, *Journal Watch* (the newsletter), and *AIDS Clinical Care*.

11 JAMA  
VOLUME 151, NUMBER 3

The Journal of Family Practice  
The Journal of the American Medical Association  
ARCHIVES OF INTERNAL MEDICINE

Volume 33, Number 6, 553-677  
Volume 267, No. 11 Pages 1429-1441

PAGES 421-628

JACC - Journal of the American College of Cardiology

Volume 19 / number 3

The American Journal of Cardiology

BRITISH MEDICAL JOURNAL

345, 349, 356

Vol 336

NO 6828 VOLUME 304

THE LANCET

Journal of Internal Medicine

Volume 116 Number 5

Please rush my **FREE** sample cassette, Volume 1, Issue 1 of **Journal Watch — The Audio Cassette Service**. If I decide to become a charter subscriber, I'll receive 9 months, 18 issues at the special introductory price of \$113.75.

NAME \_\_\_\_\_ (PLEASE PRINT)

ADDRESS \_\_\_\_\_

CITY \_\_\_\_\_

STATE \_\_\_\_\_ ZIP \_\_\_\_\_

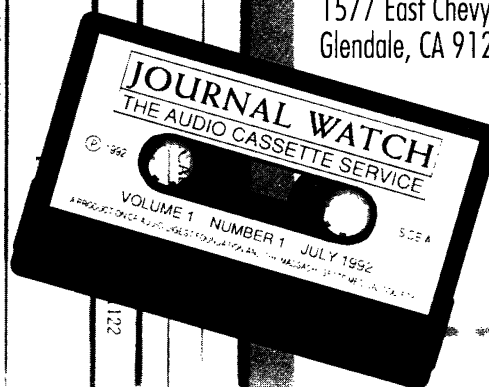
Mail to:

A Non-Profit Subsidiary of the California Medical Association  
1577 East Chevy Chase Drive  
Glendale, CA 91206

Or

(8 am to 5 pm, Pacific Time)

(24 hours)



# PRO TECTION

**MALPRACTICE COVERAGE AT ITS BEST**

- Effective and experienced management.
- An improved cash flow position immediately.
- \$1 million per occurrence/\$3 million aggregate per year.
- Affordable retroactive coverage.
- Remedial medical services designed to alleviate adverse medical/surgical results.

**COMPARE AND SAVE**

For further information, please call or write:

**PHYSICIANS**  
I N T E R I N D E M N I T Y

350 Arden Avenue, First Floor, Glendale, California 91203  
(818) 241-5119

New, for hypertension  
Once-a-day

# DILACOR XR

(diltiazem HCl) EXTENDED-RELEASE TABLETS

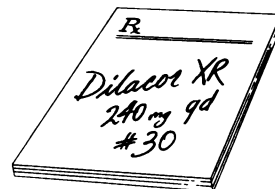


180 mg



240 mg

## 24-HOUR DELIVERY FOR 24-HOUR SECURITY



### BRIEF SUMMARY

#### CONTRAINDICATIONS

Diltiazem hydrochloride is contraindicated in: (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker; (2) patients with second or third degree AV block except in the presence of a functioning ventricular pacemaker; (3) patients with hypotension (less than 90 mmHg systolic); (4) patients who have demonstrated hypersensitivity to the drug; and (5) patients with acute myocardial infarction and pulmonary congestion as documented by X-ray on admission.

#### WARNINGS

**1. Cardiac Conduction.** Diltiazem hydrochloride prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second, or third degree AV block (22 of 10,119 patients, or 0.2%); 41% of these 22 patients were receiving concomitant  $\beta$ -adrenoceptor antagonists versus 17% of the total group. Concomitant use of diltiazem with  $\beta$ -blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single 60 mg dose of diltiazem.

**2. Congestive Heart Failure.** Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt). An acute study of oral diltiazem in patients with impaired ventricular function (ejection fraction of  $24\% \pm 6\%$ ) showed improvement in indices of ventricular function without significant decrease in contractile function (dp/dt). Worsening of congestive heart failure has been reported in patients with preexisting impairment of ventricular function. Experience with the use of diltiazem hydrochloride in combination with  $\beta$ -blockers in patients with impaired ventricular function is limited. Caution should be exercised when using this combination.

**3. Hypotension.** Decreases in blood pressure associated with diltiazem hydrochloride therapy may occasionally result in symptomatic hypotension.

**4. Acute Hepatic Injury.** Mild elevations of serum transaminases with and without concomitant elevation in alkaline phosphatase and bilirubin have been observed in clinical studies. Such elevations were usually transient and frequently resolved even with continued diltiazem treatment. In rare instances, significant elevations in alkaline phosphatase, LDH, SGOT, SGPT, and other phenomena consistent with acute hepatic injury have been noted. These reactions tended to occur early after therapy initiation (1 to 6 weeks) and have been reversible upon discontinuation of drug therapy. The relationship to diltiazem is uncertain in some cases, but probable in some others (see PRECAUTIONS).

#### PRECAUTIONS

**General.** Diltiazem hydrochloride is extensively metabolized by the liver and is excreted by the kidneys and in bile. As with any drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, oral doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with the histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these changes were reversible with continued dosing.

Dermatological events (see ADVERSE REACTIONS) may be transient and may disappear despite continued use of diltiazem hydrochloride. However, skin eruptions progressing to erythema multiforme and/or exfoliative dermatitis have also been infrequently reported. Should a dermatologic reaction persist, the drug should be discontinued.

Although Dilacor™ XR utilizes a slowly disintegrating matrix, caution should still be used in patients with preexisting severe gastrointestinal narrowing (pathologic or iatrogenic). There have been no reports of obstructive symptoms in patients with known strictures in association with the ingestion of Dilacor™ XR.

**Information for Patients.** Dilacor™ XR capsules should be taken on an empty stomach. Patients should be cautioned that the Dilacor™ XR capsules should not be opened, chewed or crushed, and should be swallowed whole.

**Drug Interaction.** Due to the potential for additive effects, caution and careful titration are warranted in patients receiving diltiazem hydrochloride concomitantly with any agents known to affect cardiac contractility and/or conduction (see WARNINGS). Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using  $\beta$ -blockers or digitalis concomitantly with diltiazem hydrochloride (see WARNINGS). As with all drugs, care should be exercised when treating patients with multiple medications. Diltiazem hydrochloride undergoes biotransformation by cytochrome P-450 mixed function oxidase. Co-administration of diltiazem hydrochloride with other agents which follow the same route of biotransformation may result in the competitive inhibition of metabolism. Dosages of similarly metabolized drugs, such as cyclosporin, particularly those of low therapeutic ratio or in patients with renal and/or hepatic impairment, may require adjustment when starting or stopping concomitantly administered diltiazem hydrochloride to maintain optimum therapeutic blood levels.

**Beta-Blockers:** Controlled and uncontrolled domestic studies suggest that concomitant use of diltiazem hydrochloride and beta-blockers or digitalis is usually well-tolerated, but available data are not sufficient to predict the effects of concomitant treatment in patients with left ventricular dysfunction or cardiac conduction abnormalities. Administration of diltiazem hydrochloride concomitantly with propranolol in five normal volunteers resulted in increased propranolol levels in all subjects and the bioavailability of propranolol was increased approximately 50%. If combination therapy is initiated or withdrawn in conjunction with propranolol, an adjustment in the propranolol dose may be warranted (see WARNINGS).

**Cimetidine:** A study in six healthy volunteers has shown a significant increase in peak diltiazem plasma levels (58%) and area-under-the-curve (53%) after a 1-week course of cimetidine at 1,200 mg per day and diltiazem 60 mg per day. Ranitidine produced smaller, nonsignificant increases. The effect may be mediated by cimetidine's known inhibition of hepatic cytochrome P-450, the enzyme system probably responsible for the first-pass metabolism of diltiazem. Patients currently receiving diltiazem therapy should be carefully monitored for a change in pharmacological effect when initiating and discontinuing therapy with cimetidine. An adjustment in the diltiazem dose may be warranted.

**Digitalis:** Administration of diltiazem hydrochloride with digoxin in 24 healthy male subjects increased plasma digoxin concentrations approximately 20%. Another investigator found no increase in digoxin levels in 12 patients with coronary artery disease. Since there have been conflicting results regarding the effect of digoxin levels, it is recommended that digoxin levels be monitored when initiating, adjusting, and discontinuing diltiazem hydrochloride therapy to avoid possible over- or under-digitalization (see WARNINGS).

**Anesthetics:** The depression of cardiac contractility, conductivity, and automaticity as well as the vascular dilation associated with anesthetics may be potentiated by calcium channel blockers. When used concomitantly, anesthetics and calcium channel blockers should be titrated carefully.

#### References:

1. Data on file, Rhône-Poulenc Rorer Pharmaceuticals Inc.
2. 1992 Drug Topics® Red Book® Update. Oradell, NJ, Medical Economics Co. Inc.; April, 1992.

**Carcinogenesis, Mutagenesis, Impairment of Fertility.** A 24-month study in rats and an 18-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response *in vitro* or *in vivo* in mammalian cell assays or *in vitro* in bacteria. No evidence of impaired fertility was observed in male or female rats at oral doses of up to 100 mg/kg/day.

**Pregnancy.** Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from 4 to 6 times (depending on species) the upper limit of the optimum dosage range in clinical trials (480 mg q.d. or 8 mg/kg q.d. for a 60 kg patient) has resulted in embryo and fetal lethality. These studies have revealed: in one species or another, a propensity to cause abnormalities of the skeleton, heart, retina, and tongue. Also observed were reductions in early individual pup weights and pup survival, prolonged delivery and increased incidence of stillbirths.

There are no well-controlled studies in pregnant women; therefore, use diltiazem hydrochloride in pregnant women only if the potential benefit justifies the potential risk to the fetus.

**Nursing Mothers.** Diltiazem is excreted in human milk. One report suggests that concentrations in breast milk may approximate serum levels. If use of diltiazem hydrochloride is deemed essential, an alternative method of infant feeding should be instituted.

**Pediatric Use.** Safety and effectiveness in children have not been established.

#### ADVERSE REACTIONS

Serious adverse reactions to diltiazem hydrochloride have been rare in studies with other formulations, as well as with Dilacor™ XR. It should be recognized, however, that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded from these studies.

The most common adverse events (frequency  $\geq 1\%$ ) in placebo-controlled, clinical hypertension studies with Dilacor™ XR using daily doses up to 540 mg are listed in the table below with placebo-treated patients included for comparison.

MOST COMMON ADVERSE EVENTS  
IN DOUBLE-BLIND, PLACEBO-CONTROLLED HYPERTENSION TRIALS\*

Adverse Events (COSTART Term)	Dilacor™ XR n=303 # pts (%)	Placebo n=87 # pts (%)
rhinitis	29 (9.6)	7 (8.0)
headache	27 (8.9)	12 (13.8)
pharyngitis	17 (5.6)	4 (4.6)
constipation	11 (3.6)	2 (2.3)
cough increase	9 (3.0)	2 (2.3)
flu syndrome	7 (2.3)	1 (1.1)
edema, peripheral	7 (2.3)	0 (0.0)
myalgia	7 (2.3)	0 (0.0)
diarrhea	6 (2.0)	0 (0.0)
vomiting	6 (2.0)	0 (0.0)
sinusitis	6 (2.0)	1 (1.1)
asthenia	5 (1.7)	0 (0.0)
pain, back	5 (1.7)	2 (2.3)
nausea	5 (1.7)	1 (1.1)
dyspepsia	4 (1.3)	0 (0.0)
vasodilatation	4 (1.3)	0 (0.0)
injury, accident	4 (1.3)	0 (0.0)
pain, abdominal	3 (1.0)	0 (0.0)
arthrosis	3 (1.0)	0 (0.0)
insomnia	3 (1.0)	0 (0.0)
dyspnea	3 (1.0)	0 (0.0)
rash	3 (1.0)	1 (1.1)
tinnitus	3 (1.0)	0 (0.0)

\*Adverse events occurring in 1% or more of patients receiving Dilacor™ XR.

The following additional events (COSTART Terms), listed by body system, were reported infrequently in all subjects and hypertensive patients who received Dilacor™ XR (n=425): Cardiovascular: First-degree AV block, arrhythmia, postural hypotension, tachycardia, pallor, palpitations, phlebitis, ECG abnormality, ST elevation; Nervous System: Vertigo, hypertonia, paresthesia, dizziness, somnolence; Digestive System: Dry mouth, anorexia, tooth disorder, eructation; Skin and Appendages: Sweating, urticaria, skin hypertrophy (nevus); Respiratory System: Epistaxis, bronchitis, respiratory disorder; Urogenital System: Cystitis, kidney calculus, impotence, dysmenorrhea, vaginitis, prostate disease; Metabolic and Nutritional Disorders: Gout, edema; Musculoskeletal System: Arthralgia, bursitis, bone pain; Hemic and Lymphatic Systems: Lymphadenopathy; Body as a Whole: Pain, unevaluable reaction, neck pain, neck rigidity, fever, chest pain, malaise; Special Senses: Amblyopia (blurred vision), ear pain.

#### OVERDOSAGE OR EXAGGERATED RESPONSE

Overdosage experience with oral diltiazem hydrochloride has been limited. The administration of ipecac to induce vomiting and activated charcoal to reduce drug absorption have been advocated as initial means of intervention. In addition to gastric lavage, the following measures should also be considered:

**Bradycardia:** Administer atropine (0.60 to 1.0 mg). If there is no response to vagal blockade, administer isoproterenol cautiously.

**High-Degree AV Block:** Treat as for bradycardia above. Fixed high-degree AV block should be treated with cardiac pacing.

**Cardiac Failure:** Administer inotropic agents (dopamine or dobutamine) and diuretics.

**Hypotension:** Vasopressors (e.g. dopamine or levaterenol bitartrate).

Actual treatment and dosage should depend on the severity of the clinical situation as well as the judgment and experience of the treating physician.

Due to extensive metabolism, plasma concentrations after a standard dose of diltiazem can vary over tenfold, which significantly limits their value in evaluating cases of overdosage.

Charcoal hemoperfusion has been used successfully as an adjunct therapy to hasten drug elimination. Overdoses with as much as 10.8 gm of oral diltiazem have been successfully treated using appropriate supportive care.

**CAUTION:** FEDERAL (U.S.A.) LAW PROHIBITS DISPENSING WITHOUT PRESCRIPTION.

Please see product circular for full prescribing information.



RHÔNE-POULENC RORER PHARMACEUTICALS INC.  
500 ARCOLA ROAD  
COLLEGEVILLE, PA 19426

Rhône-Poulenc Rorer introduces

*for hypertension*

*Once-a-day*

# DILACOR™ XR

(diltiazem HCl) EXTENDED  
RELEASE  
CAPSULES

**MEDI-CAL  
APPROVED**  
180 mg: R73080M 240 mg: R73080N



DILACOR XR effectively lowers blood pressure  
for 24 hours in the majority of patients<sup>1</sup>

DILACOR XR offers the classic diltiazem safety  
profile across the entire dosing range<sup>1</sup>

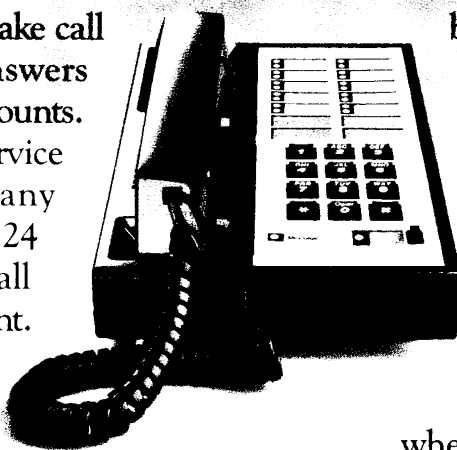
DILACOR XR makes diltiazem a cost-effective  
choice for the treatment of hypertension<sup>2</sup>

*Please see adjacent page for brief summary of prescribing information*

# INTRODUCING **ONE CALL**<sup>TM</sup> **24 HOUR BUSINESS SERVICE**

Now you don't have to make call after call searching for answers about your small business accounts. With One Call Business Service you can handle virtually any small business transaction 24 hours a day with just one call to a Wells Fargo Business Agent.

Transfer funds between accounts. Review deposits and withdrawals. Call in the payroll. You can even access your



business line of credit around the clock—only at Wells Fargo.

So if your bank has you making too many calls, save time and switch to Wells Fargo. Call 1-800-488-4000 ext. 575 for an appointment or stop by your local Wells Fargo office today.

And come to the only bank where you can do all your business banking with just one call.

©1992, WFB, N.A. Member FDIC

## WELLS FARGO BANK

Applies to California residents only.



## FREE HIV RISK ASSESSMENT PROGRAM AVAILABLE

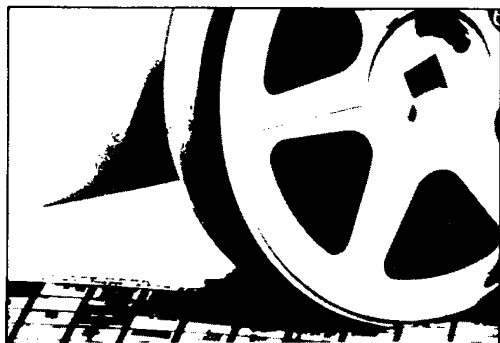
CMA's Department of Physician Education has produced a new CME program, "HIV Risk Assessment: Methods and Guidelines," which is available free to physicians. This program teaches effective strategies developed by expert physicians to identify patients who are potentially at risk for HIV infection. Worth one hour of CME Category I credit, the program is designed for groups of 5-20 physicians.

The program features CMA's award-winning, 11-minute video, "Let's Talk," which highlights several methods physicians can use to perform HIV assessment with patients. Participants receive a course outline, camera-ready slide reproductions, a compilation of state laws pertaining to HIV/AIDS, community resource guide to HIV testing and counseling, risk assessment guidelines, and a model HIV consent form and patient information pamphlet.

Those interested in taking part in this unique CME program should contact Amy Wright in CMA's Department of Physician Education at 415/882-5186.



## This Publication is available in Microform.



### University Microfilms International

Please send additional information:

For \_\_\_\_\_  
Name: \_\_\_\_\_  
Institution: \_\_\_\_\_  
Street: \_\_\_\_\_  
City: \_\_\_\_\_  
State: \_\_\_\_\_ Zip: \_\_\_\_\_

300 North Zeeb Road, Dept. P.R., Ann Arbor, MI 48106

## BuSpar<sup>®</sup> (buspirone HCl)

**References:** 1. Data on file, Bristol-Myers Squibb Company. 2. Cohn JB, Bowden CL, Fisher JG, Rodos JJ. Double-blind comparison of buspirone and clonazepam in anxious outpatients with or without depressive symptoms. *Psychopharmacology*. 1992;25:10-21. 3. Fegelson JP, Cohn JB. Analysis of individual symptoms in generalized anxiety—a pooled, multisite, double-blind evaluation of buspirone. *Neuropsychopharmacology*. 1989;21:124-130. 4. Lader M. Assessing the potential for buspirone dependence or abuse and effects of its withdrawal. *Am J Med*. 1987;82(suppl 5A):20-26. 5. Newton RE, Marunycz JD, Alderice MT, Napolitano MJ. Review of the side-effect profile of buspirone. *Am J Med*. 1986;80(suppl 3B):17-21.

**Contraindications:** Hypersensitivity to buspirone hydrochloride.

**Warnings:** The administration of BuSpar to a patient taking a monoamine oxidase inhibitor (MAOI) may pose a hazard. Since blood pressure has become elevated when BuSpar was administered concomitantly with an MAOI, such concomitant use is not recommended. BuSpar should not be employed in lieu of appropriate antipsychotic treatment.

**Precautions:** **General – Interference with cognitive and motor performance:** Although buspirone is less sedating than other anxiolytics and does not produce significant functional impairment, its CNS effects in a given patient may not be predictable; therefore, patients should be cautioned about operating an automobile or using complex machinery until they are reasonably certain that buspirone does not affect them adversely. Although buspirone has not been shown to increase alcohol-induced impairment in motor and mental performance, it is prudent to avoid concomitant use with alcohol.

**Potential for withdrawal reactions in sedative/hypnotic/anxiolytic drug dependent patients:** Because buspirone will not block the withdrawal syndrome often seen with cessation of therapy with benzodiazepines and other common sedative/hypnotic drugs, before starting buspirone withdrawal patients gradually from their prior treatment, especially those who used a CNS depressant chronically. Rebound or withdrawal symptoms may occur over varying time periods, depending in part on the type of drug and its elimination half-life. The withdrawal syndrome can appear as any combination of irritability, anxiety, agitation, insomnia, tremor, abdominal cramps, muscle cramps, vomiting, sweating, flu-like symptoms without fever, and occasionally, even as seizures.

**Possible concerns related to buspirone's binding to dopamine receptors:** Because buspirone can bind to central dopamine receptors, a question has been raised about its potential to cause acute and chronic changes in dopamine mediated neurological function (eg, dystonia, pseudoparkinsonism, akathisia, and tardive dyskinesia). Clinical experience in controlled trials has failed to identify any significant neuroleptic-like activity; however, a syndrome of restlessness, appearing shortly after initiation of treatment, has been reported; the syndrome may be due to increased central noradrenergic activity or may be attributable to dopaminergic effects (ie, represent akathisia).

**Information for Patients –** Patients should be instructed to inform their physician about any medications, prescription or nonprescription, alcohol or drugs they are now taking or plan to take during treatment with buspirone; to inform their physician if they are pregnant, are planning to become pregnant, or become pregnant while taking buspirone; to inform their physician if they are breast feeding; and not to drive a car or operate potentially dangerous machinery until they experience how this medication affects them.

**Drug Interactions –** Concomitant use with other CNS active drugs should be approached with caution (see **Warnings**). Concomitant use with trazodone may have caused 3- to 6-fold elevations of SGPT (ALT) in a few patients. Concomitant administration of BuSpar and haloperidol resulted in increased serum haloperidol concentrations in normal volunteers. The clinical significance is not clear. Buspirone does not displace tightly bound drugs like phenytoin, propranolol, and warfarin from serum proteins, but may displace less tightly bound drugs like digoxin. However, there was one report of prolonged prothrombin time when buspirone was given to a patient also treated with warfarin, phenytoin, phenobarbital, digoxin, and Synthroid.

**Carcinogenesis, Mutagenesis, Impairment of Fertility –** No evidence of carcinogenic potential was observed in rats or mice; buspirone did not induce point mutations, nor was DNA damage observed; chromosomal aberrations or abnormalities did not occur.

**Pregnancy: Teratogenic Effects –** Pregnancy Category B: Should be used during pregnancy only if clearly needed.

**Nursing Mothers –** Administration to nursing women should be avoided if clinically possible.

**Pediatric Use –** The safety and effectiveness have not been determined in individuals below 18 years of age.

**Use in the Elderly –** No unusual, adverse, age-related phenomena have been identified in elderly patients receiving a total, modal daily dose of 15 mg.

**Use in Patients with Impaired Hepatic or Renal Function –** Since buspirone is metabolized by the liver and excreted by the kidneys, it is not recommended in severe hepatic or renal impairment.

**Adverse Reactions (See also Precautions): Commonly Observed –** The more commonly observed untoward events, not seen at an equivalent incidence in placebo-treated patients, include dizziness, nausea, headache, nervousness, lightheadedness, and excitement.

**Associated with Discontinuation of Treatment –** The more common events causing discontinuation included: central nervous system disturbances (3.4%), primarily dizziness, insomnia, nervousness, drowsiness, lightheaded feeling; gastrointestinal disturbances (1.2%), primarily nausea; miscellaneous disturbances (1.1%), primarily headache and fatigue. In addition, 3.4% of patients had multiple complaints, none of which could be characterized as primary.

**Incidence in Controlled Clinical Trials –** Adverse events reported by 1% or more of 477 patients who received buspirone in four-week, controlled trials: **Cardiovascular:** Tachycardia/palpitations 1%. **CNS:** Dizziness 12%, drowsiness 10%, nervousness 5%, insomnia 3%, lightheadedness 3%, decreased concentration 2%, excitement 2%, anger/hostility 2%, confusion 2%, depression 2%. **EENT:** Blurred vision 2%. **Gastrointestinal:** Nausea 8%, dry mouth 3%, abdominal/gastric distress 2%, diarrhea 2%, constipation 1%, vomiting 1%. **Musculoskeletal:** Musculoskeletal aches/pains 1%. **Neurological:** Numbness 2%, paresthesia 1%, incoordination 1%, tremor 1%. **Skin:** Skin rash 1%. **Miscellaneous:** Headache 6%, fatigue 4%, weakness 2%, sweating/clamminess 1%.

**Other Events Observed During the Entire Premarketing Evaluation –** The relative frequency of all other undesirable events reasonably associated with the use of buspirone in approximately 3000 subjects who took multiple doses of the drug under well-controlled, open, and uncontrolled conditions is defined as follows: Frequent are those occurring in at least 1/100 patients; infrequent are those occurring in 1/100 to 1/1000 patients; and rare are those occurring in less than 1/1000 patients. **Cardiovascular –** frequent: non-specific chest pain; infrequent: syncope, hypotension, hypertension; rare: cerebrovascular accident, congestive heart failure, myocardial infarction, cardiomyopathy, bradycardia. **Central Nervous System –** frequent: dream disturbances; infrequent: depersonalization, dysphoria, noise intolerance, euphoria, akathisia, fearfulness, loss of interest, dissociative reaction, hallucinations, suicidal ideation, seizures; rare: feelings of claustrophobia, cold intolerance, stupor, slurred speech, psychosis. **EENT –** frequent: tinnitus, sore throat, nasal congestion; infrequent: redness and itching of the eyes, altered taste, altered smell, conjunctivitis; rare: inner ear abnormality, eye pain, photophobia, pressure on eyes. **Endocrine –** rare: galactorrhea, thyroid abnormality. **Gastrointestinal –** infrequent: flatulence, anorexia, increased appetite, salivation, irritable colon, rectal bleeding; rare: burning of the tongue. **Genitourinary –** infrequent: urinary frequency, urinary hesitancy, menstrual irregularity and spotting, dysuria; rare: amenorrhea, pelvic inflammatory disease, enuresis, nocturia. **Musculoskeletal –** infrequent: muscle cramps, muscle spasms, rigid/stiff muscles, arthralgias. **Neurological –** infrequent: involuntary movements, slowed reaction time; rare: muscle weakness. **Respiratory –** infrequent: hyperventilation, shortness of breath, chest congestion; rare: epistaxis. **Sexual Function –** infrequent: decreased or increased libido; rare: delayed ejaculation, impotence. **Skin –** infrequent: edema, pruritus, flushing, easy bruising, hair loss, dry skin, facial edema, blisters; rare: acne, thinning of nails. **Clinical Laboratory –** infrequent: increases in hepatic aminotransferases (SGOT, SGPT); rare: eosinophilia, leukopenia, thrombocytopenia. **Miscellaneous –** infrequent: weight gain, fever, roaring sensation in the head, weight loss, malaise; rare: alcohol abuse, bleeding disturbance, loss of voice, hiccoughs.

**Postintroduction Clinical Experience –** Rare occurrences of allergic reactions, cogwheel rigidity, dystonic reactions, ecchymosis, emotional lability, tunnel vision, and urinary retention have been reported. Because of the uncontrolled nature of these spontaneous reports, a causal relationship to BuSpar has not been determined.

**Drug Abuse and Dependence: Controlled Substance Class –** Not a controlled substance.

**Physical and Psychological Dependence –** Buspirone has shown no potential for abuse or diversion and there is no evidence that it causes tolerance, or either physical or psychological dependence. However, since it is difficult to predict from experiments the extent to which a CNS-active drug will be misused, diverted, and/or abused once marketed, physicians should carefully evaluate patients for a history of drug abuse and follow such patients closely, observing them for signs of buspirone misuse or abuse (eg, development of tolerance, incrementation of dose, drug-seeking behavior).

**Overdosage: Signs and Symptoms –** At doses approaching 375 mg/day the following symptoms were observed: nausea, vomiting, dizziness, drowsiness, miosis, and gastric distress. No deaths have been reported in humans either with deliberate or accidental overdosage.

**Recommended Overdosage Treatment –** General symptomatic and supportive measures should be used along with immediate gastric lavage. No specific antidote is known and dialyzability of buspirone has not been determined.

For complete details, see Prescribing Information or consult your Mead Johnson Pharmaceuticals Representative.

U.S. Patent Nos. 3,717,634 and 4,182,763

MJL8-4270R2

**Mead Johnson**  
PHARMACEUTICALS  
A Bristol-Myers Squibb Company  
New Jersey, U.S.A.

# BECAUSE APPROXIMATELY 60% OF PATIENTS WITH PERSISTENT ANXIETY MAY EXHIBIT DEPRESSIVE SYMPTOMS...<sup>1</sup>



Now indicated  
for the relief of  
persistent anxiety  
with coexisting  
depressive  
symptoms

Now indicated  
for the relief of  
persistent anxiety  
with coexisting  
depressive  
symptoms

Now indicated  
for the relief of  
persistent anxiety  
with coexisting  
depressive  
symptoms

Now indicated  
for the relief of  
persistent anxiety  
with coexisting  
depressive  
symptoms

Now indicated  
for the relief of  
persistent anxiety  
with coexisting  
depressive  
symptoms

Now indicated  
for the relief of  
persistent anxiety  
with coexisting  
depressive  
symptoms

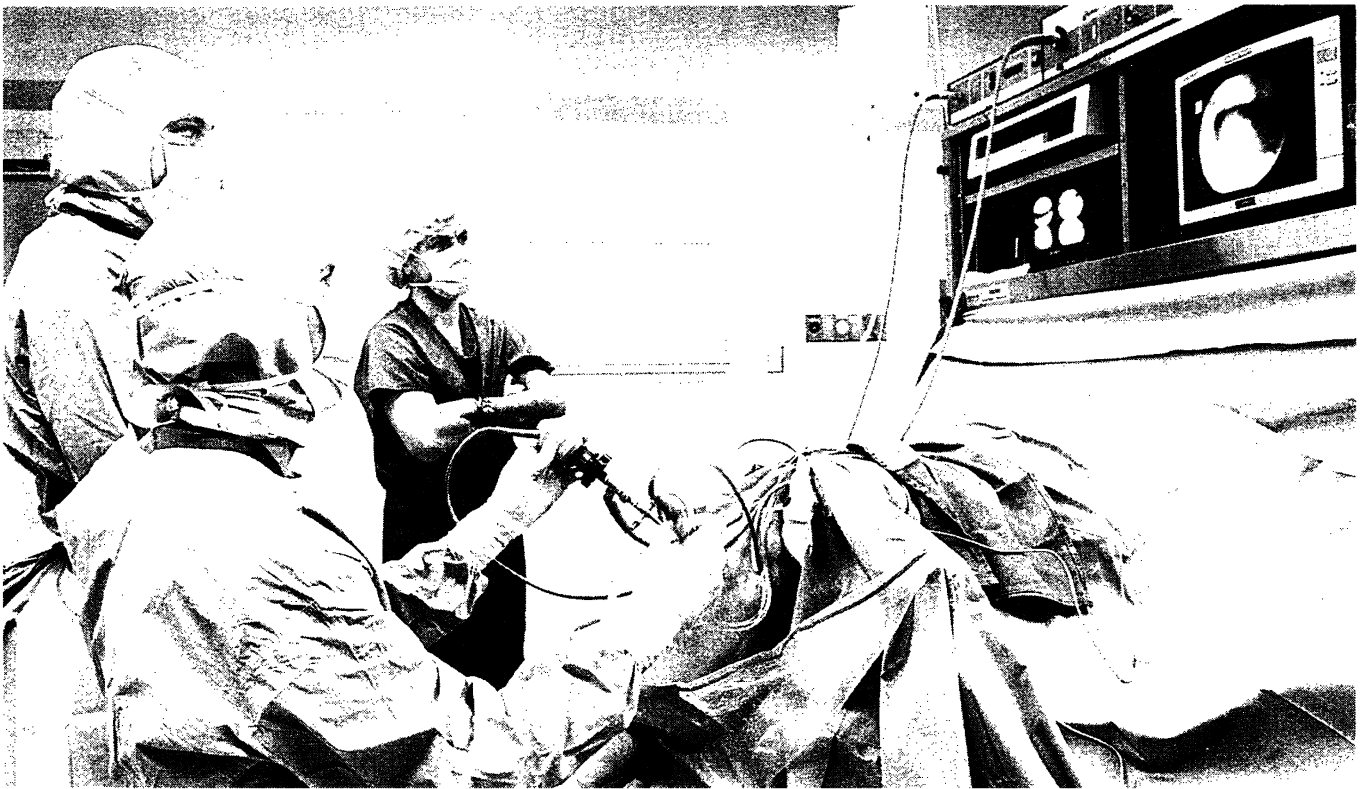
**Progressive  
Relief of  
Persistent  
Anxiety**

**\*BuSpar is not indicated for the relief of primary depressive disorder.**

Please see references and brief summary on adjacent page.

©1992, Bristol-Myers Squibb Company, Princeton, New Jersey 08543, U.S.A. JK-107

## LET ME TELL YOU ABOUT THE FIRST TIME I WAS ON TELEVISION.



As a family practice physician, Dr. Alvin Sockolov had assisted in operating room number 7 at Sutter General Hospital many times. But after re-injuring his knee, there he was, undergoing ACL surgery at the hands of Dr.



David Coward. While choosing surgery was a difficult decision, choosing Sutter General was not. "Dr. Coward prefers to operate at Sutter General," says Dr. Sockolov. "A surgeon needs special equipment, fine instruments, and a capable staff to feel comfortable. Sutter General has what physicians need for procedures to run smoothly." More orthopedic surgeries are performed at

Sutter General Hospital than at any other hospital in the region. Advanced diagnostic equipment, specially trained orthopedic nurses, and a team of rehabilitation specialists all help give Sutter General a reputation that's unmatched in Northern California. In addition, educational programs, a health library, outpatient and extended care facilities provide both physicians and patients

with the best resources available. "The only problem I had with Sutter General," says Dr. Sockolov, "was that when it came time to leave, I didn't want to go. Everything was top-notch." For more information about

available services, call Sutter Orthopedic Center at Sutter General Hospital in Sacramento, (916) 733-8880.



*Alvin Sockolov, M.D.*



**Sutter Orthopedic Center**  
SUTTER GENERAL HOSPITAL

# Classified Advertisements

The rate for each insertion is **\$7 per line** (six words per line) with **five lines (\$35) minimum**. Confidential box number charge: \$10 each month.

**Classified display rates \$60 per inch. Maximum sizes: 1 column by 9½ inches or 2 columns by 5 inches (2½ inches per column).** Larger classified ad space by special arrangements.

Copy for classified advertisements should be received not later than **25th of the second month preceding issue. All copy must be typed or printed.** • Classified advertisers using Box Numbers forbid the disclosure of their identity; your inquiries in writing will be forwarded to Box Number advertisers. Although The Western Journal of Medicine believes the classified advertisements in these columns to be from reputable sources, we do not investigate the offers made and assume no liability concerning them. The right is reserved to reject, withdraw, or modify all classified advertising copy in conformity with the decisions of the Advertising Committee.

Please Type or Print Advertising Copy

## Classified Advertisements Are Payable in Advance

CLASSIFIED ADVERTISEMENTS  
THE WESTERN JOURNAL OF MEDICINE  
P.O. BOX 7602, SAN FRANCISCO, CA 94120-7602  
(415) 882-3376  
FAX: (415) 882-3379

**OB/GYN.** Multispecialty group in northwest Washington desires second Obstetrician. Excellent practice opportunity, full range of benefits, early partnership status, all practice costs paid. For more information contact Shane Spray, 1400 E. Kincaid, Mount Vernon, WA 98273; (206) 428-2524.

**CALIFORNIA, MONTEREY BAY.** Full-/part-time positions available with Monterey Bay's largest and most successful Urgent Care network. Generous guarantee, incentive plan, and benefit package. Malpractice covered. Practice in California's most beautiful coastal recreational area. BC/BE Emergency Medicine or Family Practice specialists preferred. Contact Bob Morris, MD, FACEP, Doctors on Duty Medical Clinics, 223 Mt Hermon Rd, Scotts Valley, CA 95066; (408) 438-9341.

**WASHINGTON.** Openings for career oriented Emergency Physicians, BC in Emergency or Primary medical specialty. Seattle metropolitan hospital with 54,000 annual visits. Excellent salary in a stable growing group. Contact Dan Hiatt in care of Linda Johnson, 8009 S. 180th, Ste 110, Kent, WA 98032; (206) 575-2595.

**OTOLARYNGOLOGIST.** BC/BE to join 28 physician multispecialty group practice. Located in beautiful Pacific northwest between Seattle and Vancouver, BC. Contact Shane Spray, 1400 E. Kincaid, Mount Vernon, WA 98273.

**FAMILY PRACTICE PHYSICIAN.** Full-time in a busy walk-in medical clinic. Located in Visalia, California (Tulare County). Malpractice insurance, good salary, etc. Please call (209) 627-5555 for more information.

**ASSOCIATE IN PEDIATRICS.** Kern Medical Center, Bakersfield, California, a teaching hospital affiliated with UCLA and UCI Schools of Medicine, seeks an Associate in the Division of Pediatrics. Prerequisites include eligibility or certification by the American Board of Pediatrics, strong interest in teaching and qualifications for faculty appointment in UCLA Department of Pediatrics. Comprehensive salary and benefit package. A part-time private practice is permitted. Medical center is in central California, a mid-sized urban community with moderate cost of living. Send CV and inquiries to Navin Amin, MD, Chairman, Department of Family Practice/Pediatrics, Kern Medical Center, 1830 Flower St, Bakersfield, CA 93305.

**WANTED: BC GENERAL OR SUBSPECIALTY SURGEON** to fill the position of Chief of Surgery at a 181-bed county hospital and large ambulatory care system located in the San Francisco bay area. Responsibilities include teaching the 27 residents of the hospital-based, UC Davis-affiliated Family Practice Residency Program; assisting in the development of the Family Practice faculty; general clinical and administrative duties; and the clinical and administrative supervision of the general and subspecialty surgeons. Salary and benefits negotiable. Please send CV to Steven Tremain, MD, Director of Medical Staff Affairs, Merrithew Memorial Hospital, 2500 Alhambra Ave, Martinez, CA 94553; phone (510) 370-5110; FAX (510) 370-5142. EOE.

**SEATTLE.** As the result of population growth and reputation, this 28 physician group practice is in need of several recently trained Family Practitioners. This suburban community is situated within minutes of downtown Seattle and within one hour of Mt. Rainier. Remuneration package includes base salary plus incentive and full benefits with partnership after two years. Call rotation every 7th night and weekend. Congenial atmosphere. Contact Ken Baker, Physician Search Group, 550 Montgomery St, Ste 725, San Francisco, CA 94111; (800) 229-0411 or FAX (415) 399-0411.

## OB/GYN NORTHERN CALIFORNIA

Positions available for BC/BE OB/GYNs with private group practices in San Francisco, SF Peninsula, Marin County, and Sacramento; with multispecialty groups in South Bay. For information about these opportunities, please call **Mary Letterii** at (800) 229-0411 or (415) 399-8840 or send your CV to **Physician Search Group, 550 Montgomery St, Ste 725, San Francisco, CA 94111, FAX (415) 399-0411.** You can depend on us to handle your inquiry with complete confidence.



## PHYSICIANS NEEDED

The continuing growth of our service area population (now 105,000) has created an immediate need for additional BC/BE physicians in the following specialties:

- FAMILY PRACTICE
- ORTHOPEDIC SURGERY
- OTOLARYNGOLOGY
- PEDIATRICS
- ONCOLOGY (some general Internal Medicine necessary initially)

These excellent practice opportunities offer guaranteed income and a strong referral base.

112-bed full service hospital, very well equipped. Excellent ancillary services. Our service area population is now 105,000; a growing area with new businesses and a stable economy. A 30% plus growth in population and jobs is predicted for our area during 1990s.

Located in central California near Sequoia National park, Tulare offers an excellent family oriented lifestyle and all expected amenities. Beautiful homes, close to hospital and office, are affordably priced. Good schools, many community activities, and abundant recreation including golf, tennis, skiing, mountain and equestrian activities. Easy access to all California's major metropolitan and resort areas.

Contact:

**Tulare District Hospital  
Physician Recruiting Office  
PO Box 90112  
Los Angeles, CA 90009  
(800) 468-2687**



**GENERAL INTERNIST** in the Pacific Northwest. Busy 30 physician multispecialty group practice looking for General Internist with ICU skills and interests to join existing Internal Medicine department. Competitive salary and benefits. Send CV to Shane Spray, 1400 E. Kincaid, Mount Vernon, WA 98273.

**MAJESTIC SKAGIT VALLEY IN WESTERN WASHINGTON** has multispecialty group seeking eighth Family Practitioner. BE/BC, OB optional. Competitive salary and benefits. If interested, send CV to Shane Spray, 1400 E. Kincaid, Mount Vernon, WA 98273.

**ESCAPE** those urban hassles and come to scenic northern California and Phoenix, Arizona. Opportunity available to join two other Internists in private practice. Competitive salary and benefit package available. Contact Mark Oswald of Gielow/Laske Associates, Inc, 306 N Milwaukee St, Milwaukee, WI 53202; (800) 969-7715, FAX (414) 226-4131. Confidential inquiries welcome.

**CALIFORNIA.** The Sacramento Children's Medical Clinic, an ambulatory private practice for children of low income parents, consisting of four offices (one on wheels) needs a BE/BC General Pediatrician. Direct patient care and supervising midlevels for inner city, migrant health and outreach programs. Monday through Friday. Quake-free locale. Spectacular climate. Innumerable recreational opportunities. Competitive salary with equity potential. Contact Gilbert Simon, MD, 1355 Florin Rd, Ste 14, Sacramento, CA 95822, (916) 422-6326.

**EXCELLENT OPPORTUNITY FOR INTERNAL MEDICINE PHYSICIAN** in private practice multispecialty physician group in San Francisco. Income guarantee. No investment. Forward CV to Box 263, The Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

(Continued on Page 98)

# AIM HIGH

# CREATE A MEDICAL BREAKTHROUGH



# AIR FORCE

(Continued from Page 97)

## CALIFORNIA

Primary Care Physicians and Radiologists needed to work as *locum tenens* statewide. High salary, paid malpractice. Work whenever and wherever you wish. Permanent placements as well. **Western Physicians Registry:** Northern California, contact Jim Ellis, Director, (510) 601-7676 or (800) 437-7676. Southern California, contact Tracy Zweig, Director, (805) 643-9346 or (800) 635-3175.

**SONOMA WINE COUNTRY.** Excellent Internal Medicine opportunity. Take over existing practice; share office with associate. Finances negotiable. Salary if desired. Send CV to PO Box 1641, Sonoma, CA 95476.

**EMERGENCY MEDICINE UNIVERSITY POSITION.** The University of California, Davis, School of Medicine, is recruiting for a full-time faculty. The position will be at the Assistant or Associate Professor level. The Division of Emergency Medicine and Clinical Toxicology is undergoing rapid academic development and has an approved residency program in Emergency Medicine. The UCDMC Emergency Department provides comprehensive emergency service and is a major trauma center in Northern California. The Department is a Paramedic Base Station and Training Center, and in addition, has an active Helicopter Service and Regional Poison Center. Candidates must be BC/BE in Emergency Medicine and be eligible for licensure in California. A letter outlining teaching background, interests, experience, and research in addition to a CV and the names of five references should be sent to Robert W. Derlet, MD, Chair, Emergency Medicine Search Committee, Tr 1219, University of California, Davis, Medical Center, 2315 Stockton Blvd, Sacramento, CA 95817. Applications will not be accepted after August 1, 1992. The University of California is an Affirmative Action/Equal Opportunity Employer.

## PHYSICIANS WANTED

### SALT LAKE CITY, UTAH

Internist wanted for beautiful Salt Lake City area. Excellent skiing, camping, fishing and hunting. Looking for aggressive, hard-working Family Practitioner to expand clinic. Complete laboratory facilities and x-ray in ambulatory care type setting. Call or write: **Robert Davis, MD, Director, Family Medical Center, 1519 W. 9000 South, West Jordan, UT 84088; (801) 562-9100.**

**AMBULATORY CARE,** Hayward, Modesto, Orange County, California. Thriving practices, attractive facilities, competitive salary, profit-sharing, partnership with growth potential. Contact Robin Morgan, California Emergency Physicians, 2101 Webster St, #1050, Oakland, CA 94612; (510) 835-7431. Outside of California, (800) 842-2619.

**SALT LAKE CITY—URGENT CARE/FAMILY PRACTICE.** Six year old center in upper middle class community. BC preferred, early partnership available. Great recreation area. Work Net, PO Box 26692, Salt Lake City, UT 84199.

**NORTHERN CALIFORNIA RECREATION AREA—**Full-time and part-time salaried position in Ambulatory Care clinic. Enjoy excellent working hours, no night call, generous benefits package, malpractice insurance provided. Located near the Sierra foothills offering excellent opportunities for hiking, swimming, boating, fishing, and skiing. California license required, Family Practitioner preferred. Call or send résumé to Northern Valley Indian Health, Inc, 2167 Montgomery St, Oroville, CA 95965; (916) 534-8440. EOE. Native Americans encouraged to apply. Deadline: open until filled.

## PHYSICIANS WANTED

### Western States OPENINGS

Many multispecialty groups and hospitals have asked us to recruit for over 300 positions of various specialties. Both permanent and locum tenens. Send CV to **Western States Physician Services, 5627 E. Kings Canyon, Ste 156, Fresno, CA 93727, or call 1 (800) 873-0786.**

**BEDROOM COMMUTERS** for Los Angeles community offers full-time physician opportunity of a lifetime. Join Marina Valley Medical Group now and live the good life. Call Marcel, (714) 653-4600.

**UNIQUE OPPORTUNITY** for idealistic and ambitious private practitioner adjacent to state-of-the-art athletic/health club in Cotati, California. Family Practice, Orthopedics, or Rehabilitation Medicine. Please contact Crilly Butler, (707) 795-2141.

**NORTHERN CALIFORNIA HOSPITAL** seeking a BC/BE Internist to staff its new satellite medical clinics. Assistance is available in establishing a practice. Net income guarantees are open including support for office staff and required equipment. Contact Margaret Ward, Redbud Community Hospital, PO Box 6720, Clearlake, CA 95422; (707) 994-6486, ext 128.

**NORTHERN CALIFORNIA.** Successful solo seeks successor. Outstanding Family Practice in San Francisco suburban neighborhood. Excellent patient mix without HMO contracting. Shared call every 5th. Hospital will assist with the start-up. Contact and send CV to Ken Baker, Physician Search Group, 550 Montgomery St, Ste 725, San Francisco, CA 94111; (800) 229-0411 or FAX (415) 399-0411.

(Continued on Page 99)

(Continued from Page 99)



# R&R<sub>x</sub>

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

Dr. [Name]

## SOUTHERN CALIFORNIA Los Angeles

Chief of Staff	Oncologist
Dermatologist	Orthopedic Surgeon
Diagnostic Radiologist	Otolaryngologist
Family Physicians	Pediatricians
General Surgeon	Rheumatologist
Internists	Thoracic Surgeon
OB/GYN	Urgent Care

## ARIZONA Phoenix & Tucson

Anesthesiologists	Orthopedic Surgeons
Diagnostic Radiologists	Otolaryngologists
Family Physicians	Pathologist
Internists	Pediatricians
OB/GYNs	Urgent Care
Occupational Medicine	

As part of our team, you'll enjoy a predictable schedule. What's more, CIGNA Healthplan offers competitive salaries, comprehensive benefits, and the resources of a health care leader. For more information, call or send your CV to:

**California:** CIGNA Healthplans of CA, Professional Recruitment, 505 N. Brand Blvd., Suite 400-49, Glendale, CA 91203, (800) 468-9013.

**Arizona:** CIGNA Healthplan, Professional Staffing, 11001 N. Black Canyon Hwy, Suite 400-49, Phoenix, AZ 85029, (800) 252-2471.

CIGNA Healthplan  
**Team with results.**<sup>SM</sup>



An Equal Opportunity Employer

Classified  
Advertising  
gets  
RESULTS!



For details  
see the  
Classified  
Advertising  
form at the  
end of  
the journal.

Or call  
Classified  
Advertising:  
(415)  
882-3376.



The  
Western  
Journal  
of  
Medicine

Classified  
Advertising

### DEAR DOCTOR:

If your goals include a quality lifestyle, a dynamic medical community, excellent schools/universities, and beautiful and affordable housing, then we have the ideal practice opportunity for you!

HOLY FAMILY HOSPITAL and the MEDICAL STAFF are working together to meet the healthcare demands of our 150,000 patient population. There is an IMMEDIATE need for BC/BE physicians in the following specialties:

- FAMILY PRACTICE
- PEDIATRICS
- INTERNAL MEDICINE
- CARDIOLOGY
- PSYCHIATRY
- ORTHOPEDICS

SPOKANE, WASHINGTON (370K metro population) is the regional Healthcare and Cultural center offering a sound economy, unlimited outdoor recreation and a mild four season climate.

CONTACT with CV to: **Nancy Chaffins**



N. 5633 LIDGERWOOD  
SPOKANE, WA 99207  
(509) 482-2164  
FAX: (509) 482-2187

Classified  
Advertising is  
Affordable  
and Effective

For details see the  
Classified Advertising  
form at the end of the  
journal. Or call

Classified Advertising:  
(415) 882-3376.

(Continued on Page 101)

(Continued from Page 101)

Attractive opportunities in metropolitan and scenic recreational areas. Locations near pristine lakes, white water rivers, and national forests. Others in college communities offering professional and Big 10 college sports, fine arts, and a broad spectrum of nationally renowned CME programs. Positions available: Allergy, Dermatology, Neurosurgery, Occupational Medicine, Oncology, Orthopedics, Psychiatry, Rheumatology, and Urology. To discuss your practice preferences and these opportunities please call our toll-free number, (800) 243-4353, or send your CV to STRELCHECK & ASSOCIATES, INC, 10624 N. Port Washington Rd, Mequon, WI 53092

**PULMONARY/CRITICAL CARE.** Immediate care for BC/BE Pulmonologist to join two BC Pulmonologists/Intensivists in expanding practice located in a desirable southern California seaside community. This outstanding opportunity provides a 100% Pulmonary/Critical Care consultative practice, academic affiliations/teaching position available locally. Please reply with a letter of introduction and CV to Number 269, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

**AMBULATORY/FAMILY PRACTICE** group seeking family Practitioner/General Practitioner physician for rapidly expanding practice in northern California. Prime recreation area in growing community of 70,000. Compensation and benefits include malpractice, health insurance, and CME. Call (916) 222-2113 or send résumé to 191 Hartnell Ave, Redding, CA 96002.

**SAN FRANCISCO BAY AREA.** Two physician (with two physician assistants) General Practice/Family Practice group seeks BC/BE Family Practice, Internal Medicine or Emergency Medicine practitioner capable of General Practice, to join thriving practice in rapidly growing Tri-Valley area 40 minutes east of San Francisco. No Obstetrics. Historic wine country; sophisticated professional and suburban patient base. Competitive salary first year, with bonus potential; consideration for partnership thereafter. Will also consider minimum one year employment contract not leading to partnership. Congenial atmosphere, attractive surroundings. Excellent financial opportunity in beautiful area. Send CV to James A. Blackwell, MD, Livermore Medical Clinic, 87 Fenton St, Ste 210, Livermore, CA 94550.

**NATIONWIDE.** Urgent Care, Family Practice, and Emergency Physicians are now needed in multiple locations which include Idaho, North Carolina, Virginia, Alabama, Arizona, and more. Please send your CV to Barbara Miller, Snake River Physicians, 2995 N Cole Rd, Ste 200B, Boise, ID 83704, or call Barbara Miller at (800) 688-5008.

# Ads Get Results!

**Internal Medicine  
&  
Family Practice Physicians**

- Opportunity to develop subspecialty interests
- Excellent compensation, outstanding benefits
- Great location, unlimited recreational options
- Mortgage and relocation assistance

For more information, send your CV to: **Kaiser Permanente, SCPMG, Dept. 057, Walnut Center, Pasadena, CA 91188-8013.**

**Or Call 1-800-541-7946**

**ORTHOPEDIC SURGEONS.** Orthopedic surgeon for a very busy Orthopedic service in a 223-bed teaching hospital with residencies in General Surgery, Internal Medicine, OB/GYN, and Family Practice. Should be BC/BE. Experience in arthroscopy preferred. Salary and compensation plan negotiable depending on experience. Hospital located in beautiful northern San Joaquin Valley close to major cities and skiing areas. Please submit CV and references or contact Nathaniel Matolo, MD, Chief of Surgery, San Joaquin General Hospital, PO Box 1020, Stockton, CA 95201; phone (209) 468-6600. AA/EOE.

**SOUTHERN CALIFORNIA.** Family Practice physician position available in Riverside County. Guaranteed income, excellent benefits with early partnership. Send résumé to Number 265, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

**INTERNAL MEDICINE—NEVADA, TEXAS, LOUISIANA, FLORIDA:** Private practice opportunities available in Las Vegas and Reno, Nevada; Dallas, Victoria, and McAllen, Texas; New Orleans and Shreveport, Louisiana; West Palm Beach, Hollywood, and Plantation, Florida. For details, call Eloise Gusman, (800) 535-7698 or send CV to PO Box 101656, Ft Worth, TX 76185, or FAX (817) 927-0030.

**PEDIATRICIANS—NEVADA, CALIFORNIA, TEXAS!**  
Private practice opportunities available. Hospital sponsored with coverage or join an established group. For details, call Eloise Gusman, (800) 535-7698 or send CV to PO Box 101656, Ft Worth, TX 76185, or FAX (817) 927-0030.

**FAMILY PRACTICE—CALIFORNIA, NEVADA, LOUISIANA, AND TEXAS!** Private practice opportunities available in southern California, Las Vegas and Reno, Nevada, Shreveport and New Orleans, Louisiana with established groups. For details, call Eloise Gusman, (800) 535-7698 or send CV to PO Box 101656, Ft. Worth, TX 76185, or FAX (817) 927-0030.

**PRACTICE ON KAUAI.** Urgent Care/Family Medicine Practice in a 45 doctor quality oriented multispecialty group. Walk-in clinic in central facility plus coverage in various satellite clinics on the island. Subtropical climate, all ocean sports, golf, tennis, hiking year round. Night call not required, unless inpatient practice desired. Competitive salary, excellent benefits, congenial group. Preference given to candidate available soon. Send CV to Rex D. Couch, MD, Medical Director, Kauai Medical Group, Inc, 3420-B Kuhio Hwy, Lihue, HI 96766.

**SEATTLE, WASHINGTON. FAMILY PHYSICIAN BC/BE**, part- or full-time, wanted for a stimulating practice in a comprehensive Primary Care community clinic serving a diverse Asian/Pacific Islander population. OB required. Cantonese language skills helpful. Contact Debra Cavinta, Administrative Assistant, International District Community Health Center, 416 Maynard Ave S, Seattle, WA 98104; (206) 461-3617. EOE. Closing Date 9/30/92.

**DISCOVER IDAHO.** Urgent Care, Family Practice, and Emergency Physicians are now needed for a Low Acuity AFB Emergency Department, with an annual volume of 16K, and for an Urgent Care clinic with an annual volume of 15K. Here is your chance to live and work in one of America's fastest growing and most desirable areas. This attractive location offers the convenience and amenities of a major metropolitan area—where recreation is limited only by your imagination. Benefits include flexible scheduling, with the option of 12 or 24 hour shifts, competitive salaries, and no on-call duty. For more information please call or send your CV to Barbara Miller, Snake River Physicians, 2995 N Cole Rd, Ste 200B, Boise, ID 83704; (800) 688-5008.

**GENERAL SURGEON—PHOENIX.** A surgeon with one of the most established practices in Phoenix is seeking an associate to whom he will turn over the practice in several years. A surgeon in suburban Paradise Valley also needs an associate. For more information send CV to Gordon Crawford, Professional Recruitment, Humana Inc, Dept WJ7-2L, PO Box 1438, Louisville, KY 40201-1438, or call TOLL FREE (800) 626-1590, ext 257.

**DON'T  
FORGET!**

The deadline for submitting classifieds for the September issue of WJM is July 24. Send your advertisement to:

**Classified Advertising**  
**WJM, PO Box 7602**  
**San Francisco, CA 94120-7602**  
**(415) 882-3376**

# One Of A Kind

## Zantac®

ranitidine HCl/Glaxo 150 mg and 300 mg tablets

**Zantac® 150 Tablets**  
(ranitidine hydrochloride)

**Zantac® 300 Tablets**  
(ranitidine hydrochloride)

**Zantac® Syrup**  
(ranitidine hydrochloride)

The following is a brief summary only. Before prescribing, see complete prescribing information in Zantac® product labeling.

#### INDICATIONS AND USAGE: Zantac® is indicated in:

1. Short-term treatment of **active duodenal ulcer**. Most patients heal within four weeks.
2. **Maintenance therapy** for duodenal ulcer patients at reduced dosage after healing of acute ulcers.
3. The treatment of **pathological hypersecretory conditions** (eg, Zollinger-Ellison syndrome and systemic mastocytosis).
4. Short-term treatment of **active, benign gastric ulcer**. Most patients heal within six weeks and the usefulness of further treatment has not been demonstrated.
5. Treatment of **gastroesophageal reflux disease (GERD)**. Symptomatic relief commonly occurs within one or two weeks after starting therapy. Therapy for longer than six weeks has not been studied.

In active duodenal ulcer; active, benign gastric ulcer; hypersecretory states; and GERD, concomitant antacids should be given as needed for relief of pain.

**CONTRAINDICATIONS:** Zantac® is contraindicated for patients known to have hypersensitivity to the drug.

#### PRECAUTIONS:

**General:** 1. Symptomatic response to Zantac® therapy does not preclude the presence of gastric malignancy.

2. Since Zantac is excreted primarily by the kidney, dosage should be adjusted in patients with impaired renal function (see DOSAGE AND ADMINISTRATION). Caution should be observed in patients with hepatic dysfunction since Zantac is metabolized in the liver.

**Laboratory Tests:** False-positive tests for urine protein with Multistix® may occur during Zantac therapy, and therefore testing with sulfosalicylic acid is recommended.

**Drug Interactions:** Although Zantac has been reported to bind weakly to cytochrome P-450 *in vitro*, recommended doses of the drug do not inhibit the action of the cytochrome P-450-linked oxygenase enzymes in the liver. However, there have been isolated reports of drug interactions that suggest that Zantac may affect the bioavailability of certain drugs by some mechanism as yet unidentified (eg, a pH-dependent effect on absorption or a change in volume of distribution).

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** There was no indication of tumorigenic or carcinogenic effects in lifespan studies in mice and rats at doses up to 2,000 mg/kg/d.

Ranitidine was not mutagenic in standard bacterial tests (*Salmonella*, *Escherichia coli*) for mutagenicity at concentrations up to the maximum recommended for these assays.

In a dominant lethal assay, a single oral dose of 1,000 mg/kg to male rats was without effect on the outcome of two matings per week for the next nine weeks.

**Pregnancy: Teratogenic Effects: Pregnancy Category B:** Reproduction studies have been performed in rats and rabbits at doses up to 160 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to Zantac. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

**Nursing Mothers:** Zantac is secreted in human milk. Caution should be exercised when Zantac is administered to a nursing mother.

**Pediatric Use:** Safety and effectiveness in children have not been established.

**Use in Elderly Patients:** Ulcer healing rates in elderly patients (65 to 82 years of age) were no different from those in younger age groups. The incidence rates for adverse events and laboratory abnormalities were also not different from those seen in other age groups.

**ADVERSE REACTIONS:** The following have been reported as events in clinical trials or in the routine management of patients treated with Zantac®. The relationship to Zantac therapy has been unclear in many cases. Headache, sometimes severe, seems to be related to Zantac administration.

**Central Nervous System:** Rarely, malaise, dizziness, somnolence, insomnia, and vertigo. Rare cases of reversible mental confusion, agitation, depression, and hallucinations have been reported, predominantly in severely ill elderly patients. Rare cases of reversible blurred vision suggestive of a change in accommodation have been reported.

**Cardiovascular:** As with other H<sub>2</sub>-blockers, rare reports of arrhythmias such as tachycardia, bradycardia, atrioventricular block, and premature ventricular beats.

**Gastrointestinal:** Constipation, diarrhea, nausea/vomiting, abdominal discomfort/pain, and rare reports of pancreatitis.

**Hepatic:** In normal volunteers, SGPT values were increased to at least twice the pretreatment levels in 6 of 12 subjects receiving 100 mg qid intravenously for seven days, and in 4 of 24 subjects receiving 50 mg qid intravenously for five days. There have been occasional reports of hepatitis, hepatocellular or hepatocanalicular or mixed, with or without jaundice. In such circumstances, ranitidine should be immediately discontinued. These events are usually

#### BRIEF SUMMARY

**Zantac® 150 and 300 (ranitidine hydrochloride) Tablets**  
**Zantac® (ranitidine hydrochloride) Syrup**

reversible, but in exceedingly rare circumstances death has occurred.

**Musculoskeletal:** Rare reports of arthralgias.

**Hematologic:** Blood count changes (leukopenia, granulocytopenia, thrombocytopenia) have occurred in a few patients. These were usually reversible. Rare cases of agranulocytosis, pancytopenia, sometimes with marrow hypoplasia, and aplastic anemia have been reported.

**Endocrine:** Controlled studies in animals and man have shown no stimulation of any pituitary hormone by Zantac and no antiandrogenic activity, and cimetidine-induced gynecomastia and impotence in hypersecretory patients have resolved when Zantac has been substituted. However, occasional cases of gynecomastia, impotence, and loss of libido have been reported in male patients receiving Zantac, but the incidence did not differ from that in the general population.

**Integumentary:** Rash, including rare cases suggestive of mild erythema multiforme, and, rarely, alopecia.

**Other:** Rare cases of hypersensitivity reactions (eg, bronchospasm, fever, rash, eosinophilia), anaphylaxis, angioneurotic edema, and small increases in serum creatinine.

**OVERDOSAGE:** Information concerning possible overdosage and its treatment appears in the full prescribing information.

**DOSAGE AND ADMINISTRATION:** (See complete prescribing information in Zantac® product labeling).

**Active Duodenal Ulcer:** The current recommended adult oral dosage is 150 mg or 10 ml (2 teaspoonfuls equivalent to 150 mg of ranitidine) twice daily. An alternate dosage of 300 mg or 20 ml (4 teaspoonfuls equivalent to 300 mg of ranitidine) once daily at bedtime can be used for patients in whom dosing convenience is important. The advantages of one treatment regimen compared to the other in a particular patient population have yet to be demonstrated.

**Maintenance Therapy:** The current recommended adult oral dosage is 150 mg or 10 ml (2 teaspoonfuls equivalent to 150 mg of ranitidine) at bedtime.

**Pathological Hypersecretory Conditions (such as Zollinger-Ellison syndrome):** The current recommended adult oral dosage is 150 mg or 10 ml (2 teaspoonfuls equivalent to 150 mg of ranitidine) twice a day. In some patients it may be necessary to administer Zantac® 150-mg doses more frequently. Doses should be adjusted to individual patient needs, and should continue as long as clinically indicated. Doses up to 6 g/d have been employed in patients with severe disease.

**Benign Gastric Ulcer:** The current recommended adult oral dosage is 150 mg or 10 ml (2 teaspoonfuls equivalent to 150 mg of ranitidine) twice a day.

**GERD:** The current recommended adult oral dosage is 150 mg or 10 ml (2 teaspoonfuls equivalent to 150 mg of ranitidine) twice a day.

**Dosage Adjustment for Patients with Impaired Renal Function:** On the basis of experience with a group of subjects with severely impaired renal function treated with Zantac, the recommended dosage in patients with a creatinine clearance less than 50 ml/min is 150 mg or 10 ml (2 teaspoonfuls equivalent to 150 mg of ranitidine) every 24 hours. Should the patient's condition require, the frequency of dosing may be increased to every 12 hours or even further with caution. Hemodialysis reduces the level of circulating ranitidine. Ideally, the dosage schedule should be adjusted so that the timing of a scheduled dose coincides with the end of hemodialysis.

**HOW SUPPLIED: Zantac® 300 Tablets** (ranitidine hydrochloride equivalent to 300 mg of ranitidine) are yellow, capsule-shaped tablets embossed with "ZANTAC 300" on one side and "Glaxo" on the other. They are available in bottles of 30 (NDC 0173-0393-40) tablets and unit dose packs of 100 (NDC 0173-0393-47) tablets.

**Zantac® 150 Tablets** (ranitidine hydrochloride equivalent to 150 mg of ranitidine) are white tablets embossed with "ZANTAC 150" on one side and "Glaxo" on the other. They are available in bottles of 60 (NDC 0173-0344-42) and 100 (NDC 0173-0344-09) tablets and unit dose packs of 100 (NDC 0173-0344-47) tablets.

Store between 15° and 30° C (59° and 86° F) in a dry place. Protect from light. Replace cap securely after each opening.

**Zantac® Syrup**, a clear, peppermint-flavored liquid, contains 16.8 mg of ranitidine hydrochloride equivalent to 15 mg of ranitidine per 1 ml in bottles of 16 fluid ounces (one pint) (NDC 0173-0383-54).

Store between 4° and 25° C (39° and 77° F). Dispense in tight, light-resistant containers as defined in the USP/NF.

July 1990



### Glaxo Pharmaceuticals

DIVISION OF GLAXO INC.  
Research Triangle Park, NC 27709

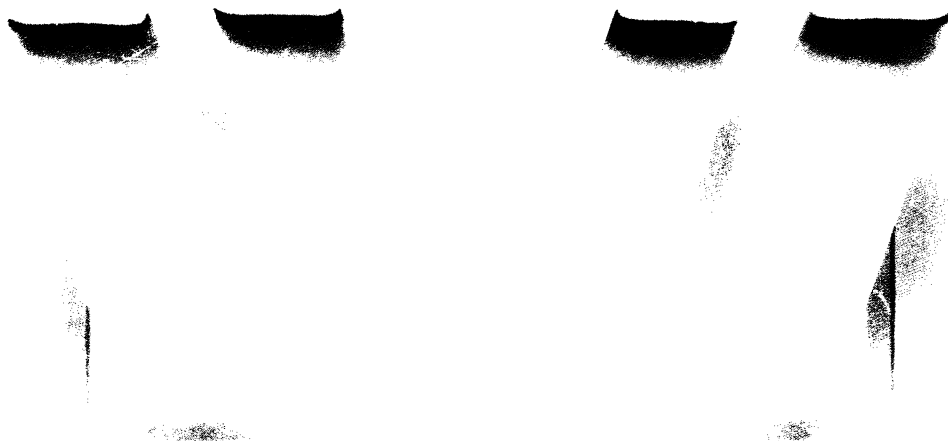
© Copyright 1987, Glaxo Inc. All rights reserved.

Medi-Cal Approved

# *One Of A Kind*



***Zantac***<sup>®</sup>  
*ranitidine HCl/Glaxo* 150 mg and  
300 mg tablets



Please see Brief Summary of Prescribing Information on adjacent page.

**Glaxo**  **ROCHE**